PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF RECEIPT OF RECORD COPY

(PCT Rule 24.2(a))

To:

WEBB, Cynthia
P.O. Box 2189
76122 Rehovot
ISRAËL

Date of mailing (day/month/year)	IMPORTANT NOTIFICATION
28 July 2000 (28.07.00)	
Applicant's or agent's file reference	**International application No.**
ALL/001	PCT/IL00/00346

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

ALLERGENE LTD. (for all designated States except US)
EISENBERG, Ronit et al (for US)

International filing date	:	14 June 2000 (14.06.00)
Priority date(s) claimed	:	17 June 1999 (17.06.99)
Date of receipt of the record copy by the International Bureau	:	03 July 2000 (03.07.00)
List of designated Offices	:	

AP :GH,GM,KE,LS,MW,MZ,SD,SL,SZ,TZ,UG,ZW
EA :AM,AZ,BY,KG,KZ,MD,RU,TJ,TM
EP :AT,BE,CH,CY,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE
OA :BF,BJ,CF,CG,CI,CM,GA,GN,GW,ML,MR,NE,SN,TD,TG
National :AE,AG,AL,AM,AT,AU,AZ,BA,BB,BG,BR,BY,CA,CH,CN,CR,CU,CZ,DE,DK,DM,DZ,EE,ES, FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KP,KR,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD, MG,MK,MN,MW,MX,MZ,NO,NZ,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,US,UZ, VN,YU,ZA,ZW

ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

- [X] time limits for entry into the national phase
- [ ] confirmation of precautionary designations
- [X] requirements regarding priority documents

A copy of this Notification is being sent to the receiving Office and to the InternationalSearching Authority.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer:
Marie-José Devillard

Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 26 February 2001 (26.02.01)	
International application No. PCT/IL00/00346	**Applicant's or agent's file reference** ALL/001
International filing date (day/month/year) 14 June 2000 (14.06.00)	**Priority date** (day/month/year) 17 June 1999 (17.06.99)
Applicant EISENBERG, Ronit et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

27 December 2000 (27.12.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer F. Baechler
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

WEBB, Cynthia
P.O. Box 2189
76121 Rehovot
ISRAËL

Date of mailing (day/month/year) 26 October 2001 (26.10.01)	
Applicant's or agent's file reference ALL/001	**IMPORTANT NOTIFICATION**
International application No. PCT/IL00/00346	**International filing date** (day/month/year) 14 June 2000 (14.06.00)

1. The following indications appeared on record concerning:

[ ] the applicant [ ] the inventor [X] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
WEBB, Cynthia P.O. Box 2189 76122 Rehovot Israel		
	Telephone No. 972-8-946-5504	
	Facsimile No. 972-8-946-5806	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
WEBB, Cynthia P.O. Box 2189 76121 Rehovot Israel		
	Telephone No. 972-8-946-5504	
	Facsimile No. 972-8-946-5806	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Marie-José DEVILLARD
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 December 2000 (28.12.2000)

PCT

(10) International Publication Number
WO 00/78346 A1

(51) International Patent Classification[7]: A61K 39/385

(21) International Application Number: PCT/IL00/00346

(22) International Filing Date: 14 June 2000 (14.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
130526 17 June 1999 (17.06.1999) IL

(71) Applicant *(for all designated States except US)*: **ALLERGENE LTD.** [IL/IL]; 2A Katzir Street, Tel Hashomer, 52656 Ramat Gan (IL).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **EISENBERG, Ronit** [IL/IL]; 6 Lotus Street, 74047 Ness-Ziona (IL). **RAZ, Tamar** [IL/IL]; 72/12 He-Beiyar Street, 48056 Rosh Haayin (IL).

(74) Agent: **WEBB, Cynthia**; P.O. Box 2189, 76122 Rehovot (IL).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/78346 A1

(54) Title: NOVEL ANTI-ALLERGIC AGENTS

(57) Abstract: The present invention discloses novel complex molecules useful as anti-allergic agents. These complex molecules include in particular, peptidic or peptidomimetic molecules, having a first segment which is competent for cell penetration and a second segment which is able to reduce or abolish mast cell degranulation, and in particular to reduce or abolish allergy mediators such as histamine secretion from mast cells. Specific examples of peptides with the desired activity are disclosed.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL00/00346

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61K 39/385
US CL :514/12,; 424/194.1; 530/317,324

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/12,; 424/194.1; 530/317,324

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DIALOG WEST MEDLINE BIOSIS EMBASE LIFESCI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ARIDOR et al. Activation of exocytosis by the heterotrimeric G protein Gi3. Science. 03 December 1993, Vol. 262, No. 5139, pages 1569-1573, see entire document.	1-48
Y	US 5,807,746 A (LIN et al) 15 September 1998, see entire document.	1-48

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 06 SEPTEMBER 2000	Date of mailing of the international search report 13 OCT 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer PATRICK J. NOLAN Telephone No (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference ALL/001/PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IL00/00346	International filing date *(day/month/year)* 14 JUNE 2000	Priority date *(day/month/year)* 17 JUNE 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 39/385 and US Cl.: 514/12,; 424/194.1; 530/317,324		
Applicant ALLERGENE LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 7 sheets.

3. This report contains indications relating to the following items:

   I [X] Basis of the report

   II [ ] Priority

   III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV [ ] Lack of unity of invention

   V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI [ ] Certain documents cited

   VII [ ] Certain defects in the international application

   VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27 DECEMBER 2000	01 JUNE 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer PATRICK J. NOLAN
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/IL00/00346

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the claims:
pages (See Attached) , as originally filed
pages _____ , as amended (together with any statement) under Article 19
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the drawings:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the sequence listing part of the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/IL00/00346

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-50	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	1-50	YES
	Claims	NONE	NO
Industrial Applicability (IA)	Claims	1-50	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claim 1-50 the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest in vivo allergy inhibition with said claimed peptides.

---------- NEW CITATIONS ----------
NONE

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-40, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) NONE, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand.
and additional amendments:
Pages 41-47, filed with the letter of 02 MAY 2001.

This report has been drawn on the basis of the drawings,
page(s) 1-14, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) NONE, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: CYNTHIA WEBB
P.O.BOX 2189
REHOVOT, ISRAEL 76122

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	21 JUN 2001

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
ALL/001/PCT	

International application No.	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/IL00/00346	14 JUNE 2000	17 JUNE 1999

Applicant
ALLERGENE LTD.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	PATRICK J. NOLAN
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/IPEA/416 (July 1992)★

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ALL/001/PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IL00/00346	International filing date *(day/month/year)* 14 JUNE 2000	Priority date *(day/month/year)* 17 JUNE 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 39/385 and US Cl.: 514/12,; 424/194.1; 530/317,324		
Applicant ALLERGENE LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 7 sheets.

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27 DECEMBER 2000	01 JUNE 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer PATRICK J. NOLAN Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/IL00/00346

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the claims:
pages (See Attached) , as originally filed
pages _____ , as amended (together with any statement) under Article 19
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the drawings:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the sequence listing part of the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/IL00/00346

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-50	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	1-50	YES
	Claims	NONE	NO
Industrial Applicability (IA)	Claims	1-50	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claim 1-50 the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest in vivo allergy inhibition with said claimed peptides.

---------- NEW CITATIONS ----------
NONE

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-40, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) NONE, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand.
and additional amendments:
Pages 41-47, filed with the letter of 02 MAY 2001.

This report has been drawn on the basis of the drawings,
page(s) 1-14, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) NONE, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: CYNTHIA WEBB
P.O.BOX 2189
REHOVOT, ISRAEL 76122

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

	Date of Mailing *(day/month/year)* 13 OCT 2000
Applicant's or agent's file reference ALL/001	**FOR FURTHER ACTION** **See paragraphs 1 and 4 below**
International application No. PCT/IL00/00346	International filing date *(day/month/year)* 14 JUNE 2000
Applicant ALLERGENE LTD.	

1. [X] The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 *bis* 1 and 90 *bis* 3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer PATRICK J. NOLAN Telephone No. (703) 308-0196

(See notes on accompanying sheet)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ALL/001	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/IL00/00346	International filing date *(day/month/year)* 14 JUNE 2000	(Earliest) Priority Date *(day/month/year)* 17 JUNE 1999
Applicant ALLERGENE LTD.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 2 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international searcl was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has bee furnished.

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (See Box II).

4. With regard to the **title**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[X] None of the figu

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL00/00346

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61K 39/385
US CL :514/12,; 424/194.1; 530/317,324
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/12,; 424/194.1; 530/317,324

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DIALOG WEST MEDLINE BIOSIS EMBASE LIFESCI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ARIDOR et al. Activation of exocytosis by the heterotrimeric G protein Gi3. Science. 03 December 1993, Vol. 262, No. 5139, pages 1569-1573, see entire document.	1-48
Y	US 5,807,746 A (LIN et al) 15 September 1998, see entire document.	1-48

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
06 SEPTEMBER 2000	13 OCT 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer PATRICK J. NOLAN Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)★

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under Article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

The statement should be brief, it should not exceed 500 words if in English or if translated into English.

It should not be confounded with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It should not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

In what language ?

The amendments must be made in the language in which the international application is published. The letter and any statement accompanying the amendments must be in the same language as the international application if that language is English or French; otherwise, it must be in English or French, at the choice of the applicant.

Consequence if a demand for international preliminary examination has already been filed ?

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase ?

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purpose of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended ?

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confounded with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

(i) the claim is unchanged;
(ii) the claim is cancelled;
(iii) the claim is new;
(iv) the claim replaces one or more claims as filed;
(v) the claim is the result of the division of a claim as filed.

CLAIMS

WHAT IS CLAIMED IS:

1. An anti-allergic complex molecule, having at least a first segment competent for importation of said molecule into mast cells in vivo, and a second segment for having an anti-allergic effect within said mast cells, said first segment being joined to said second segment through a linker, whereby the complex molecule is capable of exerting its anti-allergic effect in vivo.

2. The complex molecule of claim 1, wherein said second segment has said anti-allergic effect by at least significantly reducing degranulation of said mast cells.

3. The complex molecule of claim 2, wherein said second segment is selected from the group consisting of a peptide, a peptidomimetic and a polypeptide.

4. The complex molecule of claim 3, wherein said second segment is a peptide.

5. The complex molecule of claim 4, wherein said first segment is a peptide.

6. The complex molecule of claim 5, wherein said linker is a covalent bond.

7. The complex molecule of claim 6, wherein said covalent bond is a peptide bond.

8. The complex molecule of claim 7, wherein said molecule is a peptide

taken from the C terminal sequence of $G\alpha i_3$.

9. The complex molecule of claim 8, wherein said peptide has an amino acid sequence AAVALLPAVLLALLAPKNNLKECGLY, and cyclic derivatives thereof.

10. The complex molecule of claim 7, wherein said molecule is a peptide taken from the C terminal sequence of $G\alpha t$.

11. The complex molecule of claim 10, wherein said molecule is a peptide having an amino acid sequence AAVALLPAVLLALLAPKENLKDCGLF, and cyclic derivatives thereof.

12. A composition for treating an allergic condition in a subject, comprising a pharmaceutically effective amount of a molecule having at least a first segment competent for importation of said molecule into mast cells in vivo, and a second segment for having an anti-allergic effect within said mast cells, said first segment being joined to said second segment through a linker, whereby the complex molecule is capable of exerting its anti-allergic effect in vivo.

13. The composition of claim 12, wherein the allergenic condition is selected from the group consisting of nasal allergy, an allergic reaction in an eye of the subject, an allergic reaction in the skin of the subject, acute urticaria, psoriasis, psychogenic or allergic asthma, interstitial cystitis, bowel diseases, migraines, and multiple sclerosis.

14. The composition of claim 12, further comprising a pharmaceutically acceptable diluent or carrier.

15. The composition of claim 14, in a dosage form suitable for topical administration to the eye, the skin or to the mucous membrane of a subject.

16. The composition of claim 14, in a dosage form suitable for administration by inhalation or intranasal administration.

17. The composition of claim 14, in a dosage form suitable for oral or parenteral systemic administration.

18. The composition of claim 13, wherein said second segment has said anti-allergic effect by at least significantly reducing degranulation of said mast cells.

19. The composition of claim 18, wherein said second segment is selected from the group consisting of a peptide, a peptidomimetic and a polypeptide.

20. The composition of claim 19, wherein said second segment is a peptide.

21. The composition of claim 20, wherein said first segment is a peptide.

22. The composition of claim 21, wherein said linker is a covalent bond.

23. The composition of claim 22, wherein said covalent bond is a peptide

bond.

24. The composition of claim 23, wherein said second segment is a peptide taken from the C terminal sequence of $G\alpha i_3$.

25. The composition of claim 24, wherein said molecule is a peptide having an amino acid sequence AAVALLPAVLLALLAPKNNLKECGLY, and cyclic derivatives thereof.

26. The composition of claim 23, wherein said second segment is a peptide taken from the C terminal sequence of Gαt.

27. The composition of claim 26, wherein said molecule is a peptide having an amino acid sequence AAVALLPAVLLALLAPKENLKDCGLF, and cyclic derivatives thereof.

28. The composition of claim 27, wherein said therapeutic agent further comprises a second molecule, said second molecule being a peptide having an amino acid sequence AAVALLPAVLLALLAPKNNLKECGLY.

29. The composition of claim 20 wherein said molecule is a derivatized peptide having an amino acid sequence Succinyl-AAVALLPAVLLALLAPKNNLKECGLY.

30. A method for treating an allergic condition in a subject, comprising

administering a pharmaceutically effective amount of a therapeutic agent to the subject, said therapeutic agent comprising a molecule having at least a first segment competent for importation of said molecule into mast cells in vivo, and a second segment for having an anti-allergic effect within said mast cells, said first segment being joined to said second segment through a linker, whereby the complex molecule is capable of exerting its anti-allergic effect in vivo.

31. The method of claim 30, wherein the allergic condition is selected from the group consisting of nasal allergy, an allergic reaction in an eye of the subject, an allergic reactions in the skin of the subject, acute urticaria, psoriasis, psychogenic or allergic asthma, interstitial cystitis, bowel diseases, migraines, and multiple sclerosis.

32. The method of claim 31, wherein administration of said therapeutic agent is performed by topical administration.

33. The method of claim 32, wherein said topical administration is to the eye, the skin or to a mucous membrane of the subject.

34. The method of claim 33, wherein administration of said therapeutic agent is performed by inhalation or intranasal administration.

35. The method of claim 34, wherein administration of said therapeutic agent is performed by oral or systemic parenteral administration.

36. The method of claim 32, wherein said second segment has said anti-

allergic effect by at least significantly reducing degranulation of said mast cells.

37. The method of claim 36, wherein said second segment is selected from the group consisting of a peptide, a peptidomimetic, or a polypeptide.

38. The method of claim 37, wherein said second segment is a peptide.

39. The method of claim 38, wherein said first segment is a peptide.

40. The method of claim 39, wherein said linker is a covalent bond.

41. The method of claim 40, wherein said covalent bond is a peptide bond.

42. The method of claim 41, wherein said second segment is a peptide taken from the C terminal sequence of $G\alpha i_3$.

43. The method of claim 42, wherein said molecule is a peptide having an amino acid sequence AAVALLPAVLLALLAPKNNLKECGLY, and cyclic derivatives thereof.

44. The method of claim 41, wherein said second segment is a peptide taken from the C terminal sequence of Gαt

45. The method of claim 44, wherein said molecule is a peptide having an amino acid sequence AAVALLPAVLLALLAPKENLKDCGLF.

46. The method of claim 39, wherein said therapeutic agent further comprises a second molecule, said second molecule being a peptide having an amino acid sequence AAVALLPAVLLALLAPKNNLKECGLY.

47. The method of claim 31, wherein said molecule is a peptide having an amino acid sequence Succinyl- AAVALLPAVLLALLAPKNNLKECGLY.

48. The complex molecule of claim 8, further comprising cyclization between lysine at position 17 and the C terminus of the peptide.

49. The composition of claim 25 wherein said molecule further comprises cyclization between lysine at position 17 and the C terminus of the peptide.

50. The method of claim 31 wherein the molecule further comprises cyclization between lysine at position 17 and the C terminus of the peptide.

CLAIMS

WHAT IS CLAIMED IS:

1. An anti-allergic complex molecule having at least a first segment competent for importation of said molecule into mast cells, and a second segment for having an anti-allergic effect within said mast cells, said first segment being joined to said second segment through a linker.

2. The complex molecule of claim 1, wherein said second segment has said anti-allergic effect by at least significantly reducing degranulation of said mast cells.

3. The complex molecule of claim 2, wherein said second segment is selected from the group consisting of a peptide, a peptidomimetic, and a polypeptide.

4. The complex molecule of claim 3, wherein said second segment is a peptide.

5. The complex molecule of claim 4, wherein said first segment is a peptide.

6. The complex molecule of claim 5, wherein said linker is a covalent bond.

7. The complex molecule of claim 6, wherein said covalent bond is a peptide bond.

8. The complex molecule of claim 7, wherein said second segment is a peptide taken from the C terminal sequence of $G\alpha i_3$.

9. The complex molecule of claim 8, wherein said peptide has an amino acid sequence AAVALLPAVLLALLAPKNNLKECGLY, and cyclic derivatives thereof.

10. The complex molecule of claim 7, wherein said second segment is a peptide taken from the C terminal sequence of Gαt.

11. The complex molecule of claim 10, wherein said molecule is a peptide having an amino acid sequence AAVALLPAVLLALLAPKENLKDCGLF, and cyclic derivatives thereof.

12. A composition for treating an allergic condition in a subject, comprising as an active ingredient a pharmaceutically effective amount of a molecule having at least a first segment competent for importation of said molecule into mast cells, and a second segment for having an anti-allergic effect within said mast cells, said first segment being joined to said second segment through a linker.

13. The composition of claim 12, wherein the allergic condition is selected from the group consisting of nasal allergy, an allergic reaction in an eye of the subject, an allergic reactions in the skin of the subject, acute urticaria, psoriasis, psychogenic or allergic asthma, interstitial cystitis, bowel diseases, migraines, and multiple sclerosis.

14. The composition of claim 12, further comprising a pharmaceutically acceptable diluent or carrier.

15. The composition of claim 14, in a dosage form suitable for topical administration to the eye, the skin or to a mucous membrane of a subject.

16. The composition of claim 14, in a dosage form suitable for administration by inhalation or intranasally

17. The composition of claim 14, in a dosage form suitable for oral or parenteral systemic administration.

18. The composition of claim 13, wherein said second segment has said anti-allergic effect by at least significantly reducing degranulation of said mast cells.

19. The composition of claim 18, wherein said second segment is selected from the group consisting of a peptide, a peptidomimetic, a polypeptide, and a protein.

20. The composition of claim 19, wherein said second segment is a peptide.

21. The composition of claim 20, wherein said first segment is a peptide.

22. The composition of claim 21, wherein said linker is a covalent bond.

23. The composition of claim 22, wherein said covalent bond is a peptide bond.

24. The composition of claim 23, wherein said second segment is a peptide

taken from the C terminal sequence of $G\alpha i_3$.

25. The composition of claim 24, wherein said molecule comprises a peptide having an amino acid sequence AAVALLPAVLLALLAPKNNLKECGLY, and cyclic derivatives thereof.

26. The composition of claim 23, wherein said second segment is a peptide taken from the C terminal sequence of $G\alpha t$.

27. The composition of claim 26, wherein said molecule comprises a peptide having an amino acid sequence AAVALLPAVLLALLAPKENLKDCGLF, and cyclic derivatives thereof.

28. The composition of claim 27, wherein said therapeutic agent further comprises a second molecule, said second molecule being a peptide having an amino acid sequence AAVALLPAVLLALLAPKNNLKECGLY.

29. The composition of claim 20, wherein said molecule is a derivatized peptide having an amino acid sequence Succinyl-AAVALLPAVLLALLAPKNNLKECGLY.

30. A method for treating an allergic condition in a subject, comprising the step of administering a pharmaceutically effective amount of a therapeutic agent to the subject, said therapeutic agent comprising a molecule having at least a first segment competent for importation of said molecule into mast cells, and a second segment for

having an anti-allergic effect within said mast cells, said first segment being joined to said second segment through a linker.

31. The method of claim 30, wherein the allergic condition is selected from the group consisting of nasal allergy, an allergic reaction in an eye of the subject, an allergic reactions in the skin of the subject, acute urticaria, psoriasis, psychogenic or allergic asthma, interstitial cystitis, bowel diseases, migraines, and multiple sclerosis.

32. The method of claim 31, wherein the step of administering said therapeutic agent is performed by topical administration.

33. The method of claim 32, wherein said topical administration is to the eye , the skin or to a mucous membrane of the subject.

34. The method of claim 33, wherein the step of administering said therapeutic agent is performed by inhalation or by intranasal administration.

35. The method of claim 34, wherein the step of administering said therapeutic agent is performed by oral or systemic parenteral administration.

36. The method of claim 32, wherein said second segment has said anti-allergic effect by at least significantly reducing degranulation of said mast cells.

37. The method of claim 36, wherein said second segment is selected from the group consisting of a peptide, a polypeptide, and a protein.

38. The method of claim 37, wherein said second segment is a peptide.

39. The method of claim 38, wherein said first segment is a peptide.

40. The method of claim 39, wherein said linker is a covalent bond.

41. The method of claim 40, wherein said covalent bond is a peptide bond.

42. The method of claim 41, wherein said second segment is a peptide taken from the C terminal sequence of $G\alpha i_3$.

43. The method of claim 42, wherein said molecule is a peptide having an amino acid sequence AAVALLPAVLLALLAPKNNLKECGLY, and cyclic derivatives thereof.

44. The method of claim 41, wherein said second segment is a peptide taken from the C terminal sequence of $G\alpha t$.

45. The method of claim 44, wherein said molecule is a peptide having an amino acid sequence AAVALLPAVLLALLAPKENLKDCGLF, and cyclic derivatives thereof.

46. The method of claim 40, wherein said therapeutic agent further comprises a second molecule, said second molecule being a peptide having an amino acid sequence

AAVALLPAVLLALLAPKNNLKECGLY.

47. The method of claim 31, wherein said molecule is a peptide having an amino acid sequence Succinyl-AAVALLPAVLLALLAPKNNLKECGLY.

48. A method for promoting importation of a molecule into a cell of a subject *in vivo*, the method comprising the steps of:

(a) attaching a leader sequence to the molecule, said leader sequence being a peptide having an amino acid sequence AAVALLPAVLLALLAP, to form a complex;

(b) administering said complex to the subject; and

(c) importing said complex into the cell through said leader sequence, such that the molecule is imported into the cell.